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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/980,360	04/08/2002	Leonard C. Bailey	RU-0174	1418
26259	7590	10/17/2003		
LICATLA & TYRRELL P.C. 66 E. MAIN STREET MARLTON, NJ 08053				
			EXAMINER DI NOLA BARON, LILIANA	
			ART UNIT 1615	PAPER NUMBER

DATE MAILED: 10/17/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application N .

09/980,360

Applicant(s)

BAILEY ET AL.

Examiner

Liliana Di Nola-Baron

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 April 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-16 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-16 is/are rejected.
- 7) ☒ Claim(s) 11 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Claim Objections

1. Claim 11 is objected to because of the following informalities: the word “comprises” in line 2 should be preceded by the phrase “which” or substituted with the word “comprising”.

Appropriate correction is required.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Akagi et al. (U.S. Patent 5,723,269).

Akagi et al. provides a method to prepare microspheres having prolonged release properties (See col. 1, lines 49-67).

With respect to claim 1, the microparticles, including microspheres (See col. 1, lines 49-51), produced by the process disclosed by Akagi et al. comprise a drug entrapped in a biodegradable polymer (See col. 6, lines 32-37) and mixed with a pH adjustor, such as an alkali metal salt of an inorganic acid, including carbonic acid, and a base, such as sodium hydroxide (See col. 8, line 66

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to col. 10, line 6). Thus, the patent discloses a biodegradable microsphere comprising a biodegradable polymer and a basic excipient, as claimed by Applicant.

With regard to the method claimed in claim 6 of the instant application, Akagi et al. provides a method to prepare microspheres comprising dissolving a drug in the presence of a pH adjustor, including a salt of an inorganic acid and sodium hydroxide, and mixing said solution with a polymer solution (See col. 8, line 65 to col. 9, line 20). Akagi et al. contemplates the use of biodegradable polymers in the method of the invention (See col. 6, lines 32-37), thus the microspheres produced by the method of the invention are biodegradable. Akagi et al. teaches that the microparticles prepared by the method of the invention provide a prolonged release of the drug and exhibit longer sustained effects compared with the conventional sustained release drugs (See col. 12, lines 50-60). With regard to the limitation, that the claimed method comprises incorporating a basic excipient into a biodegradable polymer to form a microsphere and encapsulating the drug within the microsphere, the patent teaches that both the drug and the basic excipient are incorporated into the polymer (See col. 8, line 65 to col. 9, line 22). It is the view of the examiner that the "comprising" language of the claim allows for any order in the addition of the various ingredients. Furthermore, in Example 6 in Applicant's specification, a solution containing insulin and sodium bicarbonate is suspended in the polymer solution, thus the method disclosed by Applicant comprises adding the active agent and the basic excipient to the polymer, as taught by the prior art. Thus, Akagi et al. provides a method of improving the release profile of a drug encapsulated within a biodegradable microsphere, comprising including a basic excipient in the biodegradable polymer and encapsulating a drug, as claimed by Applicant.

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Regarding the method claimed in claim 11 of the instant application, Akagi et al. provides a method comprising encapsulating a drug and a basic pH adjustor, in a biodegradable polymer (See col. 8, line 65 to col. 9, line 22 and col. 6, lines 32-37), and discloses administration of the preparations of the invention to a patient in need thereof (See col. 11, line 7 to col. 12, line 44).

With regard to the limitation, that the claimed method comprises encapsulating the drug in a microsphere comprising a basic excipient and a biodegradable polymer, the patent teaches that both the drug and the basic excipient are encapsulated into the polymer (See col. 8, line 65 to col. 9, line 22). It is the view of the examiner that the "comprising" language of the claim allows for any order in the addition of the various ingredients. Furthermore, in Example 6 in Applicant's specification a solution containing insulin and sodium bicarbonate is suspended in the polymer solution, thus the method disclosed by Applicant comprises adding the active agent and the basic excipient to the polymer, as taught by the prior art. Thus, Akagi et al. provides a method of delivering a drug to a patient comprising encapsulating the drug in a biodegradable microsphere comprising a basic excipient and a biodegradable polymer and administering the encapsulated drug, as claimed by Applicant.

With regard to claims 2, 3, 7, 8, 13 and 14, Akagi et al. includes peptides having biological activity, and specifically insulin, among the drugs used in the invention (See col. 2, line 66 to col. 3, line 53).

Regarding claims 4, 9 and 15, Akagi et al. includes a copolymer of lactic acid and glycolic acid among the biodegradable polymers suitable for the invention (See col. 6, lines 32-67).

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With respect to claim 5, 10 and 16, Akagi et al. includes sodium hydrogen carbonate, also known in the art as sodium bicarbonate, among the water-soluble inorganic salts used as pH adjustors or aggregation-preventing agents in the compositions of the invention (See col. 7, lines 47-65 and col. 8, line 65 to col. 9, line 10).

With regard to claim 12, Akagi et al. contemplates parenteral administration of the compositions prepared by the method of the invention (See col. 11, lines 13-42).

The compositions and methods disclosed by Akagi et al. meet the limitations of claims 1-16 of the instant application, as the patent contemplates microspheres comprising a drug, biodegradable polymer and basic excipient, and methods of preparing and delivering said microspheres. Thus, the patent anticipates the claimed invention.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 1-16 are rejected under 35 U.S.C. 102(e) as being anticipated by Steiner et al.. (U.S. Patent 6,428,771).

Steiner et al. discloses microspheres made from biodegradable polymers and comprising a drug (See col. 1, line 62 to col. 2, line 60).

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With respect to claim 1, Steiner et al. teaches that the drug is encapsulated in the microparticles of the invention by adding the drug to a solution comprising the biodegradable polymer and bicarbonate and the particles dissociate at physiological pH (See col. 8, lines 21-49). Thus, Steiner et al. provides a biodegradable microsphere for encapsulation of a drug comprising a biodegradable polymer and a basic excipient, as claimed by Applicant.

With regard to the method claimed in claim 6 of the instant application, Steiner et al. provides a method comprising adding the drug to be encapsulated to a solution comprising the biodegradable polymer and bicarbonate (See col. 8, lines 21-26) and teaches that the method of the invention provides improved microparticles, which biodegrade at physiological pH and can be delivered to targeted locations (See col. 1, lines 26-42, col. 8, lines 38-49 and col. 10, lines 14-38). pH-dependent drug release and targeted delivery are improvements over the difficulties encountered in delivering drugs through the lungs (See col. 1, lines 26-42). Thus, Steiner et al. discloses a method of improving the release profile of a drug encapsulated in a biodegradable microsphere, as claimed by Applicant.

Regarding the method claimed in claim 11 of the instant application, Steiner et al. teaches that the drug is encapsulated in microparticles by dissolving a biodegradable polymer in bicarbonate and adding the drug to the polymer solution (See col. 8, lines 21-26), and the microparticles thus obtained can be delivered to a patient using a variety of methods (See col. 10, line 45 to col. 11, line 8).

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With respect to claims 2, 3, 7, 8, 13 and 14, Steiner et al. includes proteins or peptides, such as insulin, among the drugs encapsulated in the microspheres of the invention (See col. 1, lines 61-67 and col. 8, lines 64-65).

With regard to claims 4, 9 and 15, Steiner et al. includes poly(lactic acid), poly(glycolic acid) and copolymers thereof among the biodegradable polymers used in the invention (See col. 3, lines 7-9).

Regarding claims 5, 10 and 16, Steiner et al. provides a method of encapsulating a drug in a microsphere comprising the step of dissolving the biodegradable polymer in bicarbonate, and a composition comprising bicarbonate (See col. 8, lines 21-26).

With regard to claim 12, Steiner et al. includes administration of the compositions of the invention into the nasal passages among the methods of delivery used in the invention (See col. 10, lines 44-54). Nasal administration is a form of parenteral delivery, as claimed by Applicant.

The compositions and methods disclosed by Steiner et al. meet the limitations of claims 1-16 of the instant application, as the patent contemplates microspheres comprising a drug, biodegradable polymer and basic excipient, and methods of preparing and delivering said microspheres. Thus, the patent anticipates the claimed invention.

5. Claims 1, 2, 4, 6, 7, 9, 11-13 and 15 are rejected under 35 U.S.C. 102(e) as being anticipated by Bernstein et al. (U.S. Patent 5,912,015).

Bernstein et al. discloses compositions comprising a polymeric matrix, a biologically active agent dispersed within the matrix and a metal cation also dispersed in the matrix, and methods for modulating the release of a biologically active agent from a polymeric matrix (See col. 1, lines 40-67).

With regard to claim 1, Bernstein et al. provides a microparticle having the shape of a sphere and comprising an active agent and a metal cation dispersed in the polymer matrix, and teaches that biodegradable polymers are preferred (See col. 7, lines 38-55). Bernstein et al. teaches that microspheres of PLGA degrade in vivo and in vitro and are formed using zinc carbonate, a basic excipient, as metal cation (See Example VIII, col. 14, line 39 to col. 15, line 25). Thus, Bernstein et al. provides a biodegradable microsphere for encapsulation of a drug comprising a biodegradable polymer and a basic excipient, as claimed by Applicant.

With regard to claim 6, Bernstein et al. provides a method for modulating the release of an active agent and enhancing the control of the level of active agent released in vivo, comprising the steps of dispersing a metal cation and the active agent in the polymer matrix for forming biodegradable microspheres encapsulating the active agent (See Examples VIII-X, col. 14, line 39 to col. 17, line 3).

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With respect to claim 11, Bernstein et al. teaches that microspheres comprising an active agent encapsulated in a biodegradable polymer comprising a basic excipient are administered to a patient (See Example X, col. 16, line 25 to col. 17, line 3).

Regarding claims 2, 7 and 13, Bernstein et al. teaches that the microspheres of the invention encapsulate a protein (See Examples IX and X, col. 15, line 25 to col. 17, line 3).

With respect to claims 4, 9 and 15, Bernstein et al. discloses PLGA microspheres (See Examples IX-X, col. 15, line 25 to col. 17, line 3).

With regard to claim 12, Bernstein et al. teaches that the microspheres of the invention are administered parenterally, by injection (See Example X, col. 16, lines 56-59).

The compositions and methods disclosed by Bernstein et al. meet the limitations of claims 1, 2, 4, 6, 7, 9, 11-13 and 15 of the instant application, as the patent contemplates microspheres comprising a drug, biodegradable polymer and basic excipient, and methods of preparing and delivering said microspheres. Thus, the patent anticipates the claimed invention.

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

6. Claims 1-16 are rejected under 35 U.S.C. 102(a) as being anticipated by Steiner et al. (U.S. Patent 6,428,771).

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Steiner et al. discloses microspheres made from biodegradable polymers and comprising a drug (See col. 1, line 62 to col. 2, line 60).

With respect to claim 1, Steiner et al. teaches that the drug is encapsulated in the microparticles of the invention by adding the drug to a solution comprising the biodegradable polymer and bicarbonate and the particles dissociate at physiological pH (See col. 8, lines 21-49). Thus, Steiner et al. provides a biodegradable microsphere for encapsulation of a drug comprising a biodegradable polymer and a basic excipient, as claimed by Applicant.

With regard to the method claimed in claim 6 of the instant application, Steiner et al. provides a method comprising adding the drug to be encapsulated to a solution comprising the biodegradable polymer and bicarbonate (See col. 8, lines 21-26) and teaches that the method of the invention provides improved microparticles, which biodegrade at physiological pH and can be delivered to targeted locations (See col. 1, lines 26-42, col. 8, lines 38-49 and col. 10, lines 14-38). pH-dependent drug release and targeted delivery are improvements over the difficulties encountered in delivering drugs through the lungs (See col. 1, lines 26-42). Thus, Steiner et al. discloses a method of improving the release profile of a drug encapsulated in a biodegradable microsphere, as claimed by Applicant.

Regarding the method claimed in claim 11 of the instant application, Steiner et al. teaches that the drug is encapsulated in microparticles by dissolving a biodegradable polymer in bicarbonate and adding the drug to the polymer solution (See col. 8, lines 21-26), and the microparticles thus

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obtained can be delivered to a patient using a variety of methods (See col. 10, line 45 to col. 11, line 8).

With respect to claims 2, 3, 7, 8, 13 and 14, Steiner et al. includes proteins or peptides, such as insulin, among the drugs encapsulated in the microspheres of the invention (See col. 1, lines 61-67 and col. 8, lines 64-65).

With regard to claims 4, 9 and 15, Steiner et al. includes poly(lactic acid), poly(glycolic acid) and copolymers thereof among the biodegradable polymers used in the invention (See col. 3, lines 7-9).

Regarding claims 5, 10 and 16, Steiner et al. provides a method of encapsulating a drug in a microsphere comprising the step of dissolving the biodegradable polymer in bicarbonate, and a composition comprising bicarbonate (See col. 8, lines 21-26).

With regard to claim 12, Steiner et al. includes administration of the compositions of the invention into the nasal passages among the methods of delivery used in the invention (See col. 10, lines 44-54). Nasal administration is a form of parenteral delivery, as claimed by Applicant.

The compositions and methods disclosed by Steiner et al. meet the limitations of claims 1-16 of the instant application, as the patent contemplates microspheres comprising a drug,

biodegradable polymer and basic excipient, and methods of preparing and delivering said microspheres. Thus, the patent anticipates the claimed invention.

7. Claims 1, 2, 4, 6, 7, 9, 11-13 and 15 are rejected under 35 U.S.C. 102(a) as being anticipated by Bernstein et al. (U.S. Patent 5,912,015).

Bernstein et al. discloses compositions comprising a polymeric matrix, a biologically active agent dispersed within the matrix and a metal cation also dispersed in the matrix, and methods for modulating the release of a biologically active agent from a polymeric matrix (See col. 1, lines 40-67).

With regard to claim 1, Bernstein et al. provides a microparticle having the shape of a sphere and comprising an active agent and a metal cation dispersed in the polymer matrix, and teaches that biodegradable polymers are preferred (See col. 7, lines 38-55). Bernstein et al. teaches that microspheres of PLGA degrade in vivo and in vitro and are formed using zinc carbonate, a basic excipient, as metal cation (See Example VIII, col. 14, line 39 to col. 15, line 25). Thus, Bernstein et al. provides a biodegradable microsphere for encapsulation of a drug comprising a biodegradable polymer and a basic excipient, as claimed by Applicant.

With regard to claim 6, Bernstein et al. provides a method for modulating the release of an active agent and enhancing the control of the level of active agent released in vivo, comprising the steps

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of dispersing a metal cation and the active agent in the polymer matrix for forming biodegradable microspheres encapsulating the active agent (See Examples VIII-X, col. 14, line 39 to col. 17, line 3).

With respect to claim 11, Bernstein et al. teaches that microspheres comprising an active agent encapsulated in a biodegradable polymer comprising a basic excipient are administered to a patient (See Example X, col. 16, line 25 to col. 17, line 3).

Regarding claims 2, 7 and 13, Bernstein et al. teaches that the microspheres of the invention encapsulate a protein (See Examples IX and X, col. 15, line 25 to col. 17, line 3).

With respect to claims 4, 9 and 15, Bernstein et al. discloses PLGA microspheres (See Examples IX-X, col. 15, line 25 to col. 17, line 3).

With regard to claim 12, Bernstein et al. teaches that the microspheres of the invention are administered parenterally, by injection (See Example X, col. 16, lines 56-59).

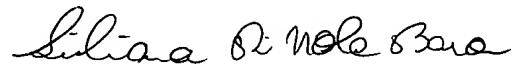
The compositions and methods disclosed by Bernstein et al. meet the limitations of claims 1, 2, 4, 6, 7, 9, 11-13 and 15 of the instant application, as the patent contemplates microspheres comprising a drug, biodegradable polymer and basic excipient, and methods of preparing and delivering said microspheres. Thus, the patent anticipates the claimed invention.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Liliana Di Nola-Baron whose telephone number is 703-308-8318. The examiner can normally be reached on Monday through Thursday, 5:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 703-308-2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 308-1234/ 1235.



October 14, 2003

Liliana Di Nola-Baron
Patent Examiner
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